IN THE UNITED STATES PATENT AND TRADEMARK OFFICE BEFORE THE BOARD OF APPEALS AND INTERFERENCES

Application of:	Jon Carl Marlowe et al.	Confirmation No.:	9078
Serial No.:	10/734,063	Art Unit:	1631
Filed:	December 10, 2003	Examiner:	Jason M. Sims
For:	AUTOMATED SYSTEM AND METHOD FOR PREPARING AN ASSAY READY BIOLOGICAL SAMPLE	Attorney Docket No.:	9301-232-999
		CAM No.:	301891-999224
		January 30, 2008	

REPLY BRIEF

Adriane M. Antler
Peter G. Thurlow
JONES DAY
222 East 41st Street
New York, New York 10017-6702
(212) 326-3939
Attorneys for Appellants

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Jon Carl Marlowe et al.	Confirmation No.:	9078
Serial No.:	10/734,063	Art Unit:	1631
Filed:	December 10, 2003	Examiner:	Jason M. Sims
For:	AUTOMATED SYSTEM AND METHOD FOR PREPARING AN ASSAY READY BIOLOGICAL SAMPLE	Attorney Docket No.:	9301-232-999
		CAM No.:	301891-999224
		January 30, 2008	

REPLY BRIEF UNDER 37 C.F.R. § 41.41

E-File
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Examiner's Answer mailed November 30, 2007, and in accordance with 37 C.F.R. § 41.41, Appellants respectfully submit this Reply Brief and request consideration of the remarks made herein. Appellants' Brief on Appeal was filed on August 7, 2007.

It is estimated that no fee is required for filing this Reply Brief. However, should the Patent and Trademark Office determine otherwise, please charge the necessary fee to Jones Day Deposit Account No. 50-3013.

REPLY TO THE EXAMINER'S ANSWER

Appellants respectfully maintain the arguments as set forth in the Brief on Appeal (hereinafter the "Appeal Brief") which was filed on August 7, 2007, and which is hereby incorporated by reference in its entirety. Furthermore, Appellants respectfully submit the following arguments in response to the Examiner's Answer (hereinafter "the Examiner's Answer" or the "Answer") to the Appeal Brief.

I. The Examiner's Response to Appellants' Arguments in Section B of the Appeal Brief Relating to Claims 14-22 is Erroneous

With respect to claims 14-22 being rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 4,780,423 ("Bluestein") in view of U.S. Patent No. 6,996,538 B2 ("Lucas"), Appellants respectfully submit that the responses in the Examiner's Answer to Appellants' arguments in section B of the Appeal Brief are erroneous.

Teaching of Bluestein

Bluestein is directed to heterogeneous fluorescence assays using controlled pore glass ("CPG") particles. In particular, the invention in Bluestein relates to improved solid supports for use in fluorescence immunoassays (col. 1, lines 8-12). Bluestein teaches that prior art immunoassays were subject to a number of difficulties. The CPG particles of Bluestein are improved solid supports that have the required sensitivity and transparency to allow them to be effectively used in fluorescence immunoassays.

Teaching of Lucas

Lucas discloses an inventory control system and methods which allow third parties to monitor company inventory via the Internet and World Wide Web, and automatically order needed items.

Appellants submit that the combination of Bluestein and Lucas does not make obvious a computer-implemented method for generating a binding-ready biological sample for a binding assay that includes the steps recited in claim 14.

Response to Examiner's Comments in the Examiner's Answer

The Examiner contends the following in the Answer:

1. Regarding step 2 of claim 14, the Examiner contends that "Bluestein teaches the second step of claim 14 at col. 8, lines 10-31" (Answer, page 4, first paragraph).

2. Regarding step 3 of claim 14, the Examiner contends that "Bluestein teaches the third step of claim 14 at col. 8, lines 61-69 and col. 9, lines 1-30" (Answer, page 4, first paragraph). The Examiner states that Bluestein "discusses the use of the Screen Machine System manufactured by Pandex Laboratories as the choice of a method for generating a binding-ready biological sample."

3. Regarding step 4 of claim 14, the Examiner contends that "[a]t col. 9, lines 8-13, Bluestein *et al.* discusses a microprocessor that can be programmed for generating work instructions for generating biological samples, such as adding wash solutions and reagents" (Answer, page 4, first paragraph).

4. Regarding step 5 of claim 14, the Examiner contends that "[a]t col. 9, lines 13-15, Bluestein discusses the execution of work instructions for generating the biological sample using the SCREEN MACHINE" (Answer, page 4, first paragraph).

Appellants submit that each of the above contentions is incorrect, because the Examiner has misconstrued the claims. In particular, the Examiner has misconstrued the meaning of "generating" a binding-ready biological sample, which word "generating/generate" appears in steps 2-5 of claim 14. In particular, the Examiner appears to have misconstrued "generating" as meaning the same as "adding" or "depositing" or "positioning," which is clearly not the case, and which is contrary to the applicable law governing this issue.

Appellants submit that the Examiner has misinterpreted "generating/generate" in claim 14, inconsistent with its ordinary meaning in the art and usage in the specification, and contrary to applicable case law. More specifically, when construing claims, the Court of Appeals for the Federal Circuit has held that, during examination, the pending claims must be given their broadest reasonable interpretation which is consistent with the specification and with the interpretation that those skilled in the art would reach. *See In re Hyatt*, 211 F.3d 1367, 1372, 54 U.S.P.Q.2d 1664, 1667 (Fed. Cir. 2000); *see also In re Cortright*, 165 F.3d 1353, 1358, 49 U.S.P.Q.2d 1464, 1468 (Fed. Cir. 1999). In particular, as stated in *In re Cortright*, "[a]lthough the PTO must give claims their broadest reasonable interpretation this interpretation must be consistent with the one that those skilled in the art would reach." *In re*

Cortright, 165 F.3d at 1358 (*citing In re Morris*, 127 F.3d 1048, 1054, 44 USPQ2d, 1023, 1027 (Fed.Cir.1997)). This the Examiner has not done.

Regarding the meaning of "generating," this term is not defined in the specification. However, this term has a well-known, notorious meaning in the art, where "to generate" is defined as "to bring into existence; cause to be; produce."[1] Moreover, this well-known meaning in the art is entirely consistent with the usage of "generate" in the specification. See, e.g., the Example at pages 20-23 of the specification as filed, wherein the binding-ready biological samples are generated by, *inter alia*, amplifying, purifying, and labeling RNA.

As noted above, claim 14 recites "generating" or "generate" in the following steps 2-5 of the claim:

- preparing an experiment design for **generating** a binding-ready biological sample to be used in said binding assay;
- choosing a robot method for **generating** said binding-ready biological sample;
- generating work instructions for **generating** said binding-ready biological sample based on said experiment design and said robot method; and
- executing said work instructions on robot stations to **generate** the binding-ready biological sample.

Thus, an experiment design, robot method, and work instructions, all for **generating** a binding-ready biological sample, are elements of the claimed invention of claim 14.

In lieu of the correct interpretation of the word "generating," it is clear that the Examiner's above contentions are incorrect. In particular, Bluestein nowhere discloses a computer-implemented method for **generating** a biological sample; or preparing a experiment design, or choosing a robot method, or generating or executing work instructions, for **generating** a binding-ready biological sample.

Regarding the Examiner's first contention, that step 2 of claim 14 is disclosed at col. 8, lines 10-31 of Bluestein, this section of Bluestein describes how Example 2 was conducted. As discussed in the Appeal Brief (page 6, first paragraph),

> Examples 1 and 2 describe an embodiment of a well-known immunoassay configuration, i.e., a sandwich immunoassay (see col. 6, lines 39-53). In this sandwich immunoassay, anti-ferritin antibody

[1] See *e.g.*, Dictionary.com [http://dictionary.reference.com/browse/generate (accessed January 28, 2008)] definition of "generate," where this is definition 1 for "generate." Appellants acknowledge that this web page is not in the prior art, but Appellants submit that the meaning of "generate" has not changed since December 2002, Appellants' earliest priority date.

> coupled to glass particles is one end of the "sandwich" (col. 6, lines 61-65), which is then bound to the ferritin (the analyte being measured) in the sample which forms the "center" of the "sandwich" (col. 6, lines 29-30), which in turn is bound to a fluorescein labeled anti-ferritin antibody (col. 6, lines 49-54) (the other end of the "sandwich"). Thus, as would be clear to one of ordinary skill in the art, Bluestein describes a sandwich immunoassay in which anti-ferritin antibody bound to glass particles, and anti-ferritin antibody bound to fluorescein, bind at distinct sites to ferritin in the sample. It is the binding of these three components that is the performance of the immunoassay carried out by the SCREEN MACHINE as taught in col. 9 of Bluestein.

Appellants thus submit, as stated in the Appeal Brief, that the "binding-ready biological sample" in Example 2 of Bluestein are the ferritin standards that are incubated with each of the two anti-ferritin antibodies, one of which antibody has a fluorescein label and one of which antibody has a CPG particle attached to it. The Examiner disagrees that ferritin is the binding-ready biological sample and instead contends that "the CPG reagent of Bluestein [] is considered to be the 'binding-ready biological sample'" (Answer, page 7, first 2 lines). Presumably, by "CPG reagent," the Examiner is referring to the anti-ferritin antibody bound to the CPG particle. However, Appellants submit that, **regardless** of whether ferritin or the "CPG reagent" is the binding-ready biological sample, Bluestein still does not disclose or suggest preparing an experiment design, choosing a robot method, generating work instructions, or executing work instructions on robot stations, **for generating** (i.e., producing, bringing into existence, causing to be) a binding-ready biological sample. Thus, for example, Bluestein does not disclose any automated production of the fluorescein labeled antibody (e.g., labeling of the antibody) or of the CPG tagged-antibody (e.g., by attaching the CPG to the antibody). Applicants also emphasize that, per the recitation of claim 14, the binding-ready biological sample is a substance **to be used in a binding assay**. In particular, step 2 specifies "a binding-ready biological sample to be used in said binding assay" and steps 3-5 refer to "said" or "the" binding-ready biological sample recited in step 2.

To reiterate, the Examiner contends that step 2 of claim 14 is disclosed at col. 8, lines 10-31. Here, Bluestein discloses that the "assay protocol, materials, and equipment of Example 1 were used with the following changes ... solid phase (CPG) antiferritin antibody was employed to which was added ... sample." "To use", "to employ" and "to add" are clearly not the same as "to generate" (i.e., produce or bring into existence). Bluestein further discloses in the cited text that "[a]fter a 15 minute incubation, samples were washed ... and centrifuged." Thus, in the performance of the immunoassay, after binding of the CPG-labeled antibody, unbound antibody was washed away; then the second antibody of the

"sandwich" was added and unbound antibody washed away: "200 µl of a fluorescein labelled anti-ferritin antibody were added to each tube. Following an incubation, samples were washed ..., reconstituted ... and read...." The foregoing quoted portions of text have nothing to do with generation of either the ferritin-containing standards or the CPG reagent. Moreover, the text has to do with the performance of the immunoassay itself (i.e., determining binding of antibody to antigen) rather than "generation" of any binding-ready biological samples to be used in the immunoassay. Thus, there is no disclosure here in Bluestein of generating a binding-ready biological sample, much less preparing an experiment design to do so.

Regarding the Examiner's second contention above, that step 3 of claim 14 is disclosed at col. 8, lines 61-69 and col. 9, lines 1-30, this is also clearly incorrect in lieu of the proper construction of "generating." Col. 8, lines 61-69, merely discloses "the use" of the solid supports (CPG particles) in an automated fluorescence immunoassay system, and that certain assay configurations were used. As discussed above "use" is not "generation." Col. 9, lines 1-12, discloses that the SCREEN MACHINE performs immunoassays, and in doing so, employs solid supports, and can be programmed to add reagents and wash solutions. Performing immunoassays, and **using** solid supports are not **generating** binding-ready biological samples to be used in a binding assay. Generating does not mean the same as performing or using. Similarly, **adding** reagents is not **generating** reagents, since "to add" does not mean the same thing as "to generate." Similarly, "adding wash solutions" is clearly not the same as "generating a binding-ready biological sample"; "to add" is not "to generate" and a wash solution is not a binding-ready biological sample (under the Appellants' or Examiner's interpretation of the term). Col. 9 lines 12-16 of Bluestein discloses that the SCREEN MACHINE was used to perform the immunoassay of Examples 1 and 2, using the same materials. Col. 9, lines 16-30, discloses that CPG reagent was added to each well, followed by standard (the ferritin), and that after an incubation, fluorescein labeled anti-ferritin antibody was added, followed by incubation, washing, concentration, and reading of epifluorescence. As noted above, "adding" or "placing" is not the same as "generating." Moreover, **washing** away of unbound antibody is clearly not **generating** a binding-ready biological sample to be used in a binding assay (regardless of whether the sample is ferritin, as Appellants contend, or CPG-labelled antibody, as the Examiner contends).

Regarding the Examiner's third contention above, that step 4 of claim 14 is disclosed at col. 9, lines 8-13 of Bluestein, this is also clearly erroneous. The disclosure at col. 9, lines

8-13 is discussed above. The cited text clearly does not disclose generation of a binding-ready biological sample, much less generating work instructions to do so.

Regarding the Examiners' fourth contention above, that step 5 of claim 14 is disclosed at col. 9, lines 13-15 of Bluestein, this is also clearly erroneous. The disclosure at col. 9, lines 13-15 is discussed above. The cited text clearly does not disclose generation of a binding-ready biological sample, much less executing work instructions for generating a binding-ready biological sample on robot stations.

The Examiner also cites to col. 6, lines 35-48, col. 8, lines 10-67, and col. 9, lines 1-30 of Bluestein, in support of the § 103 rejection. The disclosures of col. 8, lines 10-31 and 61-69 and of col. 9, lines 1-30 are addressed above. Regarding col. 6, lines 35-48 and col. 8, lines 32-60, these sections of Bluestein also provide no hint or suggestion of generating a binding-ready biological sample, and thus no hint or suggestion of steps 2-5 of claim 14. Col. 6, lines 35-48 discloses that a radioimmunoassay was performed and describes the two-site ("sandwich") configuration of the immunoassay. In particular, it discloses that the sample, anti-ferritin radiolabeled antibody, and CPG-coupled anti-ferritin antibody are incubated together, followed by removal and washing of the solid phase (the CPG), and then measuring the radiolabel attached to the CPG (via the ferritin bridge between the two antibodies). "Use" and "performance" of an immunoassay, including washing of the bound antigen-antibody complex, are not the same as **"generating" (i.e. producing, bringing into existence)** a binding-ready biological reagent **to be used** in the immunoassay (as specified in step 2 of claim 14). Col. 8, lines 32-60 merely discloses and discusses the results of the assay of Example 2 described at col. 8, lines 9-31, discussed above, and thus does not remedy the deficiencies in disclosure already discussed above.

In summary, as shown by the discussion above, nothing in Bluestein discloses or suggests a computer-implemented method for the **generation** of a binding-ready biological sample, much less steps of preparing an experiment design, choosing a robot method generating work instructions, or executing work instructions on robot stations, all for **generating** a binding-ready biological sample.

The Examiner makes certain additional statements regarding Bluestein that are erroneous. In particular, the Examiner contends that Appellants' allegation that "nowhere in Bluestein is there any hint or suggestion of using the SCREEN MACHINE system, or any other method, to **generate the binding-ready biological samples to be used in the immunoassay"** (Answer, page 9, second paragraph) is not found persuasive "as the claims

do not actually recite method steps of '*generating the binding ready biological samples to be used in the immunoassay*'" (Answer page 9, third paragraph). Appellants respectfully submit that the Examiner is incorrect, since Appellants' claimed method **does** recite, e.g. in step 5: "executing said work instructions [for generating said binding-ready biological sample, per step 4] on robot stations to generate the binding-ready biological sample" which is a computer-implemented step of generating the binding-ready biological sample, and moreover, step 2 of claim 14, which provides the antecedent basis for the binding-ready biological sample of step 5, specifies that the binding-ready biological sample is "to be used in said binding assay." Thus, claim 14 does recite a method step that is automated and that generates the binding-ready biological sample to be used in a binding assay.

Regarding claim 20, the Examiner further contends that "some of the limitations" of this claim are disclosed by Bluestein at col. 4, lines 62-69 and col. 5, lines 1-4, where allegedly "Bluestein discusses the biological sample as being a receptor tissue protein" (Answer, page 5, lines 2-3). Appellants submit that Bluestein states therein that "[t]he invention [using CPG particles as improved solid supports] can be used in all types of fluorescence assays which employ a ligand and a specific binding partner to the ligand, including, without limitation, assays in which the ligand or the specific binding partner is an immunoglobulin, a DNA probe, *a receptor tissue protein*, a hormone, a drug, or the like." (col. 4, line 64, to col. 5, line 2) (emphasis added). Claim 20 specifies acquiring a tissue sample. In contrast, Bluestein discloses that a binding partner in an assay can be a receptor protein from tissue. Firstly, a protein is not a tissue sample; tissue has a meaning, commonly known in the art, that is "a group of similar cells united to perform a specific function."[2] Secondly, acquiring a sample of tissue is clearly not the same as using a particular type of protein in an assay.

Regarding claim 22, the Examiner contends that Bluestein teaches "some of the limitations" of claim 22, at col. 4, lines 62-68 and col. 5, lines, 1-4, where allegedly "Bluestein also discusses the assay as comprising a ligand and a specific binding partner to the ligand, which is a type of hybridization assay" (Answer, page 5, lines 3-4). Appellants submit that a person of ordinary skill in the art would understand that hybridization, as recited in claim 22 is the process of hybridizing, where "to hybridize" means "to form a double-stranded nucleic acid of two single strands of DNA or RNA, or one of each, by allowing the

[2] See *e.g.*, "Online Medical Dictionary" [http://cancerweb.ncl.ac.uk/cgi-bin/omd?action=Search+OMD&query=tissue accessed January 28, 2008] which states this definition of "tissue." Appellants acknowledge that this web page is not in the prior art, but Appellants submit that the meaning of "tissue" has not changed since December 2002, Appellants' earliest priority date.

base pairs of the separate strands to form complementary bonds,"[3] based on its well-known meaning in the art and usage in the specification. Appellants note that the specification of the present application describes hybridization consistent with the foregoing definition, at page 13, lines 6-8 of paragraph 63, which states, "[i]n a preferred application, two complementary strands of DNA, or a strand of DNA with a strand of RNA, interact (hybridize) to form a double-stranded nucleic acid molecule." Based on the proper construction of the term "hybridization assay," mere disclosure of a ligand and a specific binding partner to the ligand would not suggest a hybridization assay to a person of ordinary skill in the art.

For the reasons stated above and as described in the Appeal Brief, Appellants submit that Bluestein does not disclose or suggest to a person of ordinary skill in the art the features of the claimed invention of claims 14-22.

Appellants note that the Examiner rejected claims 14-22 under 35 U.S.C. § 103(a) as obvious over Bluestein in view of Lucas. Appellants submit that Lucas discloses an inventory control system and methods which allow third parties to monitor company inventory via the Internet and World Wide Web, and automatically order needed items. Appellants submit that Lucas does not remedy any of the deficiencies discussed above in regard to Bluestein since it is directed to an inventory control system and does not teach or suggest to a person of ordinary skill in the art a computer-implemented method for generating a binding-ready biological sample for a binding assay that includes the steps recited in claim 14. In regard to Lucas, the Answer states that "the Lucas reference was not used to remedy any of the deficiencies discussed above in regard to Bluestein as the above discussion only pertained to claim 14...." (Answer, page 12, first paragraph). Appellants agree that Lucas does not remedy the deficiency of Bluestein in failing to disclose the generation of a binding-ready biological sample to be used in a binding assay, including steps of preparing an experiment design, choosing a robot method, generating work instructions, and executing work instructions, for such generation. Appellants also note that Lucas is non-analogous art, and thus is not properly combined with Bluestein.

In regard to the Supreme Court's decision in *KSR International Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 167 L. Ed. 2d 705 (2007) in relation to the pending claims, the Supreme Court has stated that one should "... determine whether there was an apparent reason to combine the known elements in the fashion claimed ...." *KSR International Co.*, 127 S. Ct.

[3] See *e.g.*, Dictionary.com [http://dictionary.reference.com/browse/hybridization (accessed January 30, 2008)] definition of "hybridization," where this is definition 6 for "hybridize." Appellants acknowledge that this web page is not in the prior art, but Appellants submit that the meaning of "hybridize" has not changed since December 2002, Appellants' earliest priority date.

at 1741, 167 L. Ed. at 722. Appellants point out that neither Bluestein nor Lucas teach any of steps 2-5 of claim 14, as discussed above, since neither Lucas nor Bluestein teach preparing an experiment design, choosing a robot method, generating work instructions based on the experiment design and robot method, or executing work instructions on robot stations, **to generate** a binding-ready biological sample to be used in a binding assay. Thus, these elements of the claim are not "known elements." Moreover, the Examiner has come forward with no common sense reason or motivation to overcome this gap in the art in order to achieve the claimed invention. Therefore, even in light of the Supreme Court's KSR decision, Appellants submit that claims 14-22 are patentable over the cited prior art.

For the reasons provided above, Appellants submit that the Examiner's contentions are erroneous, and Appellants respectfully request that the rejection of claims 14-22 be reversed.

Respectfully submitted,

Date: January 30, 2008

Adriane M. Antler

Adriane M. Antler Reg. No. 32,605

JONES DAY
222 East 41st Street
New York, New York 10017
(212) 326-3694